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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,671	12/10/2001	Otfried Kistner	V-262.00	2215

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EXAMINER
BROWN, STACY S

ART UNIT	PAPER NUMBER
1648	7

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,671	KISTNER ET AL.	
	Examiner	Art Unit	
	Stacy S Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *18-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-17 in Paper No. 6, filed March 19, 2003 is acknowledged and entered. Claims 1-25 are pending. Claims 18-25 are withdrawn from consideration being drawn to non-elected inventions. Claims 1-17 are pending and examined on the merits.

Election/Restrictions

2. In response to the restriction requirement, Applicant mainly traverses that there is no serious burden on the Office to examine all groups encompassing claims 1-25. However, the groups are classified separately and would therefore require different searches in the literature. Such a search would be burdensome. Therefore, the restriction requirement is deemed proper and made FINAL.

Specification

3. The disclosure is objected to because of the following informalities: Several of the tables and examples contain incorrect notation of numerical values, for example, table 1. It appears that commas should be replaced by periods. Please also see table 3, example 3 and page 55 relating to the same problem. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 is drawn to a method for production of purified Ross River virus antigen, however the method steps fail to indicate that an antigen is recovered. The method results in the production of virus, not specifically virus antigen. Is the whole virus recovered or separate antigens of the virus?
- Claims 3-6 and 10-13 recite ranges "between about 0.3 and about 1.5" and "between about 0.1 and 0.5". These ranges are unclear and fail to point out the metes and bounds of the ranges.
- Claim 7, "reduces nucleic acid contaminants at least about 35 fold" lacks comparative basis. To what standard is the 35-fold reduction compared with?
- Claim 12, "said filtering step (d)" lacks antecedent basis in claim 8.
- Claim 13, the first and second filter appear to be reversed with regard to their respective pore size ranges. In previous claims, the pore size ranges decreased from the first filter to the second filter. Clarification is requested.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making an *immunogenic composition* of Ross River virus,

does not reasonably provide enablement for making a *vaccine*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The breadth of the claim is unreasonable because it encompasses the production of a vaccine that protects against infection by any strain in any subject susceptible to Ross River virus (RRV) infection. The nature of the invention is a viral vaccine comprising purified, inactivated RRV to protect against infection by administering to a subject susceptible to infection. The state of the art with regard to Ross River virus, evidenced by Harley et al (Clin. Micro. Review, 14:909-932) shows that while there are methods to detect RRV, there are no treatments for infection besides treating symptoms, see page 916. Harley discloses that little is known regarding human risks for infection and disease caused by RRV (page 928). Aaskov and Yu (references AF and AM cited in the information disclosure statement, PTO-1449) disclose development of candidate RRV vaccines. The methods they use to produce virus differ from the claimed method with regard to the filtration step, however, the end result is a virus that immunizes against RRV. The candidates show an immune response in mice against several of the RRV strains known, however there is no correlation between the mice model for RRV and the response in humans, lacking evidence to the contrary. The level of predictability in the art for RRV vaccines has not been established because Aaskov says that it is expected that natural exposure to RRV would result in protection from subsequent infection, yet they were unable to distinguish between natural and vaccine infection (page 1400, second column). Therefore, given a) the lack of working examples, b) the lack of direction provided to use the RRV as a protective vaccine in an accepted model for human RRV infection, c) the level of predictability in the art

regarding RRV vaccines, d) the state of the art (only symptoms are treated according to Harley), e) the breadth of the claims, and f) the unestablished level of predictability in the art, it would require undue experimentation to make and use the RRV produced in the claimed method for a vaccine protective against all strains of RRV in any susceptible host. Applicant is enabled for a method of making an immunogenic composition comprising RRV.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubensky Jr. et al (5,789,245) in view of Yu et al (reference AM from IDS).

The claims are drawn to a method for production of purified Ross River Virus antigen comprising the steps of infection in VERO cells, for example, culture/propagation, harvest and filtration. Additionally, the method of production can include a step of treating the virus filtered with a nucleic acid degrading agent having DNase and RNase activity, and inactivation of the virus. The filters have pore sizes in the ranges of between about 0.3 and about 1.5, and between about 0.1 and 0.5. The filtering reduces nucleic acid contaminants at least about 35 fold. The resulting preparation has less than about 10 pg of cellular nucleic acid per 1 microgram of virus antigen.

Dubensky teaches a large-scale method for producing alphavirus vectors by infecting VERO cells (col. 2, line 5) and incubating and propagating in a bioreactor. The media is passed through a 0.8-micron filter and then through a 0.65-micron filter to clarify the crude alphavirus particles. After concentration of the filtrate, DNase is added to digest exogenous DNA (col. 120, example 10). The virus particles are then used for various applications, including pharmaceuticals. Representative viruses that can be produced in this same manner are disclosed beginning in column 11, line 54. Among those that are suitable for the method is Ross River Virus vectors.

Dubensky's method is drawn to a large-scale production of recombinant alphavirus *vectors*. However, Yu teaches a RRV product that is suitable for eliciting an immune response, which is not a vector. One would have had a reasonable expectation of success that the recombinant alphavirus vectors of Dubensky and the virus of Yu would have similar production methods. It would have been obvious to make the product of Yu with Dubensky's method. One would have been motivated to make large quantities of RRV for immunogenic compositions and for candidate vaccine research given the lack of treatment for RRV according to Harley (see 112, 1st paragraph, scope enablement rejection). Dubensky is silent on the inactivation of RRV particles post-filtration because Dubensky's vector is inactivated at the genetic level, col. 2, lines 66-67. The production of Yu's virus with Dubensky's method would have required inactivation after filtration because Yu's virus is not a recombinant vector.

Dubensky is silent on VERO cells grown in serum-free medium, however, large-scale methods are known to require serum free medium to reduce any possible interference with

antigenicity, evidenced by other methods of large-scale production of viruses in US patents 4,525,349 and 4,664,912.

Dubensky is silent on the reduction of contaminants by 35-fold resulting in less than about 10 pg of cellular nucleic acid per 1 microgram of virus antigen. However, the step of adding DNase in Dubensky's method is equivalent to adding DNase in Applicant's method. One would expect that the steps to reduce contaminants with DNase are functionally equivalent.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

7. No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy S. Brown, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 6:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SSB
Stacy S. Brown
April 17, 2003

James C. Housel 4/21/03
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